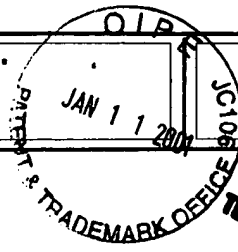


**TRANSMITTAL LETTER
(General - Patent Pending)**



Sheet No.
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In Re Application Of: **MULLER AND PECK**

... 16 2001

TECH CENTER 1600/2000

Serial No.
09/647,290

Filing Date
November 28, 2000

Examiner
Not Yet Assigned

Group Art Unit
1615

Title: **TRANSDERMAL THERAPEUTIC SYSTEM WHICH CONTAINS A d2 AGONIST AND WHICH IS PROVIDED FOR TREATING PARKINSONISM, AND A METHOD FOR THE PRODUCTION THEREOF**

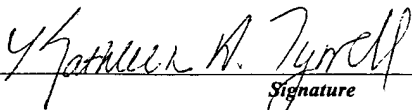
TO THE ASSISTANT COMMISSIONER FOR PATENTS:

Transmitted herewith is:

Translation of International Preliminary Examination Report

in the above identified application.

- ☒ No additional fee is required.
- ☐ A check in the amount of _____ is attached.
- ☒ The Assistant Commissioner is hereby authorized to charge and credit Deposit Account No. **50-1619** as described below. A duplicate copy of this sheet is enclosed.
- ☐ Charge the amount of _____
- ☐ Credit any overpayment.
- ☒ Charge any additional fee required.

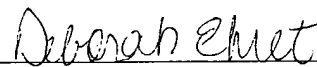

Signature

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Dated: **January 5, 2001**

I certify that this document and fee is being deposited **Jan. 5, 2001** with the U.S. Postal Service as first class mail under 37 C.F.R. 1.8 and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.



Signature of Person Mailing Correspondence

Deborah Ehret

Typed or Printed Name of Person Mailing Correspondence

CC:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Translation

Applicant's or agent's file reference	FOR FURTHER ACTION See- Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP99/01795	International filing date (day/month/year) 18 March 1999 (18.03.99)	Priority date (day/month/year) 30 March 1998 (30.03.98)
International Patent Classification (IPC) or national classification and IPC A61K 9/70		
Applicant LTS LOHMANN THERAPIE-SYSTEME AG		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
- ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
- These annexes consist of a total of 5 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 06 October 1999 (06.10.99)	Date of completion of this report 30 June 2000 (30.06.2000)
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP99/01795

I. Basis of the report

1. This report has been drawn on the basis of (Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.):

- ☐ the international application as originally filed.
- ☒ the description, pages 1-3,5-8,10-15, as originally filed,
pages _____, filed with the demand,
pages 4,4a,9, filed with the letter of 19 May 2000 (19.05.2000),
pages _____, filed with the letter of _____.
- ☒ the claims, Nos. 11(part).12-17, as originally filed,
Nos. _____, as amended under Article 19,
Nos. _____, filed with the demand,
Nos. 1-10, 11(part), filed with the letter of _____,
Nos. _____, filed with the letter of _____.
- ☒ the drawings, sheets/fig 1/1, as originally filed,
sheets/fig _____, filed with the demand,
sheets/fig _____, filed with the letter of _____,
sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/fig _____

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

4. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP 99/01795

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	2-17	YES
	Claims	1	NO
Inventive step (IS)	Claims	2-17	YES
	Claims	1	NO
Industrial applicability (IA)	Claims	1-17	YES
	Claims		NO

2. Citations and explanations

The following documents are referred to:

- D1: SWART P.J. et al.: "The influence of azone on the transdermal penetration of the dopamine D2 agonist N-0923 in freely moving rats", INT. J. PHARM. (1992), 88(1-3), 165-70, XP002110532
- D2: CHIANG C.M. et al.: "A two-phase matrix for the delivery of N-0923, a dopamine agonist", PROC. INT. SYMP. CONTROLLED RELEASE BIOACT. MATER. (1995), 22ND, 710-11, XP002110533
- D3: WO-A-94/07468 (CYGNUS THERAPEUTIC SYSTEMS), 14 April 1994 (1994-04-14) (cited in the application)

It is not clear from the cited literature whether the designation N-0923 represents the active ingredient (-)-5,6,7,8-tetrahydro-6-[propyl[2-(2-thienyl)ethyl]amino-1-naphthol in the free base form or the hydrochloride form (see document D1, page 165, right-hand column, line 3; page 166, right-hand column, last paragraph; and page 169, left-hand column, fifth line from the bottom).

Since Examples 1-7 in the present application show that the claimed transdermal therapeutic systems (TTS) are produced both with the active ingredient in the free base form (Examples 1 and 2) and also with the hydrochloride with the addition of oleic acid (Example 3) or a base (Examples 4-7), the designation (-)-5,6,7,8-tetrahydro-6-[propyl[2-(2-thienyl)ethyl]amino-1-naphthol (Claim 1, line 3) encompasses both the free base and the hydrochloride.

The phrase "solubility for the free D2 agonist base" merely defines the suitability of the matrix; it does not indicate anything about the form of the active ingredient in the matrix layer.

Document D1 discloses a TTS for (-)-5,6,7,8-tetrahydro-6-[propyl[2-(2-thienyl)ethyl]amino-1-naphthol hydrochloride which (at least when *in situ*) has a silicone-based matrix with the active ingredient (page 166, right-hand column, last paragraph; and page 168, left-hand column, first paragraph). By contrast with the present application, however, the matrix is not self-adhesive (page 168, left-hand column, first paragraph).

Document D2 describes a simple matrix system for the transdermal release of N-0923, consisting of a solution of the active ingredient and additives in a silicone adhesive which is applied to a protective film and has a polyester backing film (page 710, left-hand column, third paragraph; also page 711, Table 1). Document D2 is therefore prejudicial to the novelty of Claim 1 of the present application (PCT Article 33(2)).

Document D3 discloses two-phase matrix systems for S(-)-2-(N-propyl-N-2-thienylethylamine)-5-hydroxytetralin for transdermal application, consisting of a backing layer, a matrix layer and a protective film. The hydrophobic matrix layer is based on a silicone adhesive in which are dispersed 5% active ingredient, calcium silicate powder and an emulsifier (page 15, Example 16, lines 31-34). Since the matrix system described in D3 is a non-aqueous silicone-based polymer adhesive system, D3 is prejudicial to the novelty of Claim 1 of the present application (PCT Article 33(2)).

The subject matter of Claims 2-18 appears to be novel and inventive (PCT Article 33(2) and (3)).

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

If N-0923 represents (-)-5,6,7,8-tetrahydro-6-[propyl[2-(2-thienyl)ethyl]amino-1-naphthol hydrochloride, the vertical axis of the graph in the drawing is incorrectly labelled and unclear (PCT Article 6) because the active ingredient used in Examples 1 and 2 is the free base, not the salt.